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Silent Left Ventricular Dysfunction During Routine Activity After Thrombolytic Therapy for Acute Myocardial Infarction

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To investigate prospectively the occurrence and significance of postinfarction transient left ventricular dysfunction, 33 ambulatory patients who underwent thrombolytic therapy after myocardial infarction were monitored continuously for 187 ± 56 min during normal activity with a radionuclide left ventricular function detector at the time of hospital discharge. Twelve patients demonstrated 19 episodes of transient left ventricular dysfunction (>0.05 decrease in ejection fraction, lasting ≥1 min), with no change in heart rate. Only two episodes in one patient were associated with chest pain and electrocardiographic changes. The baseline ejection fraction was 0.52 ± 0.12 in patients with transient left ventricular dysfunction and 0.51 ± 0.13 in patients without dysfunction (p = NS). At follow-up study (19.2 ± 5.4 months), cardiac events (unstable angina, myocardial infarction or death) occurred in 8 of 12 patients with but in only 3 of 21 patients without transient left ventricular dysfunction (p < 0.01). During submaximal supine bicycle exercise, only two patients demonstrated a decrease in ejection fraction ≥0.05 at peak exercise; neither had a subsequent cardiac event.

These data suggest that transient episodes of silent left ventricular dysfunction at hospital discharge in patients treated with thrombolysis after myocardial infarction are common and associated with a poor outcome. Continuous left ventricular function monitoring during normal activity may provide prognostic information not available from submaximal exercise test results.

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The importance of silent myocardial ischemia in stable coronary artery disease, acute myocardial infarction and unstable angina pectoris is recognized (1–4). In contrast, little is known concerning the incidence and clinical relevance of silent ischemia after thrombolysis for acute myocardial infarction. Silent ischemia most frequently has been defined by electrocardiographic (ECG) ST segment changes. However, experimental and clinical studies (5–11) indicate that changes in left ventricular performance may be more sensitive than the ECG for detecting myocardial ischemia. Recently (12–14), a new device has been developed to record left ventricular function continuously in ambulatory patients. This previously validated technique (12–16) uses the principles of equilibrium-gated radionuclide angiocardiography and offers a valuable means of monitoring ventricular performance in patients during routine activities.

The present study was undertaken to evaluate prospectively the occurrence of left ventricular dysfunction during routine predischarge hospital activity in patients who received thrombolytic therapy after myocardial infarction. The observed relevance of transient abnormalities in ventricular performance was related to subsequent cardiac events and compared with left ventricular response to supine submaximal bicycle exercise stress.

Methods

Study patients. All male patients enrolled in phase II-B of the Thrombolysis in Myocardial Infarction (TIMI) Trial at Yale University School of Medicine (December 1986 through May 1988) were eligible to participate in this study at the time of TIMI protocol predischarge equilibrium radionuclide angiocardiography. Female patients were excluded because of potential technical difficulties of positioning the ventricular function monitor over the breast.

Eligibility criteria included chest pain >30 min, ECG ST segment elevation >0.1 mV in at least two leads reflecting a single myocardial region and <4 h from onset of chest pain

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Table 1. Clinical Characteristics of the 33 Patients Undergoing Ventricular Function Monitoring During Routine Activity

	Transient Left Ventricular Dysfunction	
	Present (n = 22)	Absent (n = 21)
Age (yr)	60 ± 10	53 ± 10
Previous MI	3	4
Rest LVEF	0.52 ± 0.12	0.51 ± 0.13
Anterior MI	3	12
Inferior MI	9	9
Rest BP (mm Hg)	138/84	119/72*
Beta-blocker therapy	8	14
Ca channel blocker therapy	7	10
Angiographic variables (n = 20)		
Multivessel disease	2	4
Coronary angioplasty	5	9

*$p < 0.05$. Absent = patients with no decrease in left ventricular ejection fraction (LVEF) with monitoring during routine activity; BP = blood pressure; Ca = calcium; MI = myocardial infarction; Present = patients with episodes of >0.05 decrease in left ventricular ejection fraction with monitoring during routine activity.

to the initiation of therapy. Exclusion criteria have been previously reported (17).

A total of 33 patients were included (Table 1). Thirteen additional eligible patients were not included: six refused, four could not participate for logistic reasons involving equipment availability and three had technically inadequate recording of left ventricular function data. The protocol was approved by the Human Investigation Committee of this institution. All patients gave informed consent.

The diagnosis of myocardial infarction was confirmed by myocardial creatine kinase elevation or development of new Q waves in all patients. Eighteen patients underwent coronary angiography before the left ventricular function study. In 14 of these patients, percutaneous transluminal coronary angioplasty of the infarct-related artery was performed; six patients did not have suitable coronary anatomy as defined by the study protocol (18). The rest radionuclide left ventricular ejection fraction at hospital discharge for the entire study group was 0.51 ± 0.13 (range 0.26 to 0.74). Twenty-two patients were receiving a beta-adrenergic blocker (metoprolol; mean dose 115 ± 68 mg), and 17 patients were receiving a calcium channel blocker.

Protocol. All patients were treated with 100 mg of intravenous recombinant tissue-type plasminogen activator (rt-PA) (Genentech) infused over 6 h. Patients were randomized to undergo coronary angioplasty at 18 to 48 h after thrombolytic therapy or to have no angioplasty. Those without specified contraindications to beta-blocker therapy were also randomized to receive immediate beta-blocker therapy versus beta-blocker therapy at day 6 (19). Standard contraindications to beta-blocker use were employed in the randomization and have been previously reported (19). Patients not eligible for immediate beta-blocker therapy were reassessed at day 6, and then started on beta-blocker therapy if clinically eligible. Intravenous heparin therapy to maintain the partial thromboplastin time at 1.5 to 2 times control was employed for the first 5 days; subcutaneous heparin therapy was continued thereafter until exercise testing. All patients were treated with aspirin (80 mg/day), and this was increased to 325 mg/day when heparin was discontinued. Other medication was prescribed as clinically indicated. A calcium channel blocker was routinely administered after angioplasty.

As part of the TIMI protocol, patients underwent equilibrium radionuclide angiocardiography at rest and during supine bicycle exercise between 24 and 48 h before hospital discharge (usually 7 to 10 days after admission). Monitoring with the ventricular function detector during routine activity was performed 45 to 60 min after this test, and did not require additional administration of any radiopharmaceutical. Monitoring was started for all patients between 12:00 noon and 1:00 PM. Submaximal exercise thallium-201 scintigraphy was also obtained in 22 patients when logistically possible after bicycle exercise and before hospital discharge.

Exercise equilibrium radionuclide angiocardiography. A modified in vivo technique was used to label red blood cells (20). Patients underwent imaging on a bicycle ergometer tilted between 0 and 30°, with the gamma camera positioned in the left anterior oblique view that provided optimal separation of the ventricles. Two 2 min acquisitions were averaged to obtain a baseline rest left ventricular ejection fraction value. Ejection fraction was calculated from the time-activity curve generated with an automated edge detection algorithm (21). Patients subsequently performed graded bicycle exercise in 3 min stages for a maximum of 9 min, starting at 200 kp-m and increasing by 200 kp-m at each stage. Radionuclide data were acquired for the last 2 min of each stage. Patients were monitored with a 12 lead ECG, and blood pressure was measured at the end of the stage. Exercise was terminated if the patient had a heart rate of 120 to 130 beats/min, symptoms (fatigue, chest pain, hypotension, dyspnea, leg pain) or 2 mm ST segment depression. Regional wall motion was assessed visually at rest and at peak exercise (22).

Exercise thallium-201 scintigraphy. Patients performed submaximal treadmill exercise in 3 min stages for a maximum of 9 min (2.5 mph, 12% grade). The test was terminated using the same criteria used for bicycle exercise; 1.5 to 2 min before the end of exercise, 2 mCi of thallium-201 was injected intravenously. Myocardial imaging was performed within 5 min after exercise and at redistribution 2 to 2.5 h later in the left anterior oblique, anterior and left lateral views for 8 min/view. Qualitative and quantitative analysis was performed by techniques previously validated and described (23); lung uptake was assessed qualitatively (24).

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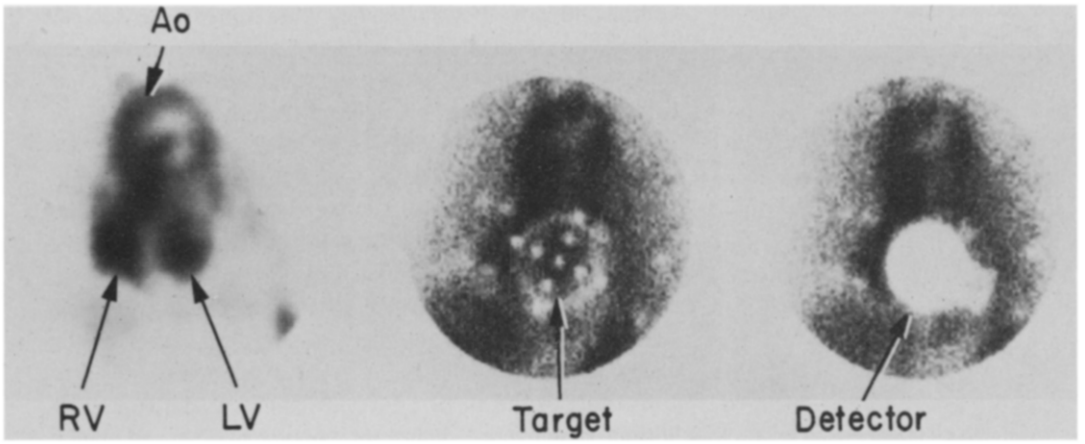

Figure 1. Static imaging in the left anterior oblique position demonstrating positioning of the VEST. **Left panel,** Blood pool images showing the right and left ventricles. The blood pool appears dark; the aorta (Ao) appears as a dark structure, whereas the interventricular septum appears as a light structure between the left (LV) and right (RV) ventricles. **Middle panel,** Positioning the target over the left ventricular blood pool. The target consists of two lines of 1 cm lead markers that are 1 cm apart arranged perpendicular to each other to form an X. The target is centered over the left ventricle by both angulating and moving the mounting bracket. The target fits in the same bracket as the VEST detector and can be removed and replaced with the VEST detector without changing the position or orientation of the mounting bracket. **Right panel,** The target has been replaced by the detector, which is seen over the left ventricle and obscuring underlying blood pool radioactivity.

Significant ECG changes for both exercise tests were defined as ≥1 mm flat or downsloping ST segment depression in three consecutive beats measured at 0.08 s after the J point.

Continuous ejection fraction monitoring (VEST). The left ventricular function monitoring system (VEST, Capintec) consists of a nonimaging detector, a modified Holter recorder and a small microprocessor that provides timing and ECG gating information (12–16). The detector is a 5.5 cm diameter sodium iodide crystal with a parallel hole collimator, mounted on a semirigid plastic vest-type garment that serves to keep it in a fixed position relative to the heart. A cadmium telluride detector is used to monitor background over the right lung field to assess changes in background that might cause artifactual changes in ejection fraction. A two channel ECG timing signal and radionuclide data are continuously recorded on Holter cassette tape. The VEST detector weighs 0.75 kg and is supported by the VEST garment, which weighs 0.8 kg. The associated electronic ware carried by the patient weighs 2.1 kg. The nuclear data consist of sequential gamma counts of left ventricular activity which are obtained 32 times/s and digitized and recorded on tape. The tape is subsequently read into a dedicated minicomputer (PDP 11/73, DEC; IBM PC/RT, IBM) for further analysis.

Data acquisition with the VEST was begun approximately 45 to 60 min after exercise testing, at a time when vital signs and findings on the ECG had returned to baseline values. Electrocardiographic leads were placed on the chest to record modified leads II and V_5. A standard gamma camera study to determine a baseline ejection fraction value was obtained with the patient sitting upright. The VEST garment was then placed around the patient's chest, and the detector was centered over the left ventricle using a positioning target (Fig. 1).

Baseline data were obtained for 5 to 10 min, with the patient sitting upright. The mean variability of absolute ejection fraction for serial 30 s-averaged data obtained over the first 4 min of this time period was ±0.021. Data were then recorded during normal ambulatory activity. Patients were asked to wear the VEST for 3 to 4 h; however, it was removed earlier if it was too uncomfortable. Patients kept a detailed log of all events, activities, symptoms and changes in position during the monitoring time; they refrained from lying down or raising their arms over their heads (maneuvers that potentially change the position of the detector relative to the heart). In 20 patients, at the conclusion of monitoring, quality control static gamma camera images to document the final detector position and a left anterior oblique-gated radionuclide angiocardiogram were obtained with the patient seated upright.

Continuous ejection fraction monitoring data analysis. A background factor was determined to equate VEST baseline ejection fraction to that of sitting upright gamma camera ejection fraction. Because background monitored over the right lung field did not change significantly during monitoring in any patient, this constant factor was then applied in the subsequent analysis of ejection fraction. This method has been validated in previous studies (13–15). The radionuclide data, gated with the ECG, were summed for 15 to 30 s intervals, and ejection fraction, decay-corrected relative ventricular volumes, heart rate and ST segment changes were calculated for the monitoring period. End-diastolic

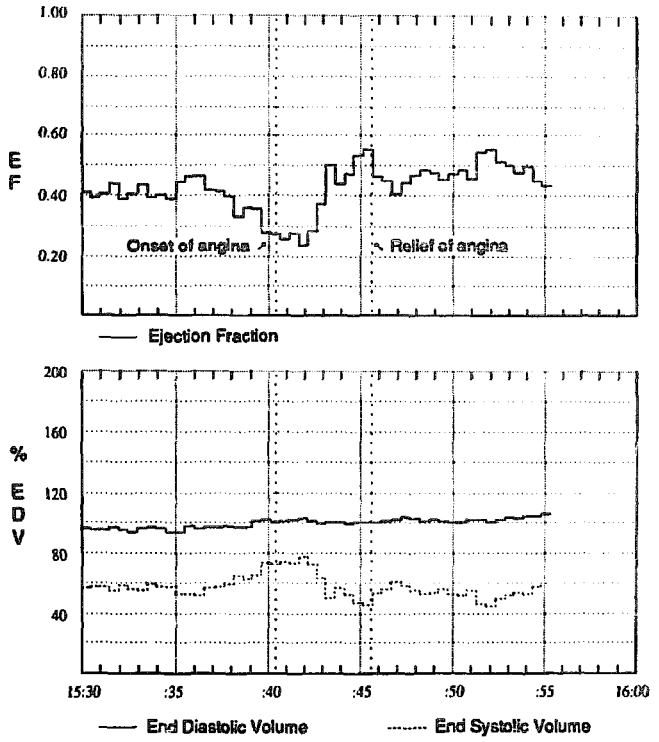

Figure 2. Trended display of ejection fraction (EF) (upper panel) and relative end-diastolic and end-systolic volumes (lower panel) during an episode of ischemia. End-systolic volume is expressed relative to end-diastolic volume (EDV). There is an episode of major left ventricular dysfunction (decrease in left ventricular ejection fraction) occurring between 15:38 and 15:44. There is no change in relative end-diastolic volume, whereas end-systolic volume increases with left ventricular dysfunction. The decrease in left ventricular ejection fraction occurs before the onset of angina.

volume was considered to be 100% at the beginning of the study and subsequently expressed relative to this initial value; end-systolic volume was expressed relative to end-diastolic volume. Any ST segment changes were measured at 80 ms after the J point, and compared with the preceding PR segment measured from 60 to 20 ms before the onset of the QRS complex. These data were calculated and displayed over time in graphic manner (Fig. 2).

On the basis of data from normal volunteers in our laboratory and others (13), the variability of ejection fraction expressed as the standard deviation of mean left ventricular ejection fraction for serial 30 s-averaged data obtained during minimal or no activity was 0.03. Thus, a decrease in ejection fraction >0.05 was 2 standard deviations from normal variability and was considered to reflect significant left ventricular dysfunction; no normal subject demonstrated a decrease in ejection fraction of this magnitude. This value is in close accord with the 0.05 decline considered to be significant during conventional radionuclide exercise testing and with the variability assessed in cardiac patients at rest (25,26). Decreases in ejection fraction were considered abnormal only if lasting ≥1 min. Investigators (1–4,27–29) using ST segment changes as evidence for silent ischemia have employed a similar time to exclude possible artifacts.

All data were analyzed blinded to clinical course and outcome. Analysis of all exercise data was performed independently.

Follow-up. Patients have been followed up for 19.2 ± 5.4 months (range 8.3 to 26). Cardiac events were defined as recurrent myocardial infarction, unstable angina requiring hospitalization or intervention or sudden death.

Statistics. Data are expressed as mean values ± 1 SD. Comparisons between groups were performed using Student's *t* test or Fisher's exact test. Cox proportional hazards regression analysis was used to test for difference in clinical outcome in patients with and without left ventricular dysfunction during routine activity, adjusting for age and unequal length of follow-up period. All p values are two-tailed; statistical significance was achieved at the 5% level ($p < 0.05$).

Results

Continuous left ventricular function monitoring (Table 1). The mean duration of left ventricular function monitoring was 187 ± 56 min. Twelve patients demonstrated 19 episodes of left ventricular dysfunction; the remaining 21 had no episodes or dysfunction. Both groups of patients were monitored for the same time (178 ± 66 versus 192 ± 49 min, p = NS). The patients with transient left ventricular dysfunction had a slightly higher blood pressure at rest than did those without such dysfunction. There was no difference between the two groups in patients undergoing coronary angioplasty at 18 to 48 h. Only one patient had chest pain during the monitoring period; this patient was also the only one manifesting ECG ST segment changes. The mean duration of episodes of left ventricular dysfunction was 4.5 ± 3.0 min (range 1 to 15). There was no significant change in heart rate during these episodes (baseline 79 ± 12 versus 85 ± 25 beats/min during dysfunction, p = NS). The mean heart rate during dysfunction was in part elevated as a result of one episode of supraventricular tachycardia at 170 beats/min; if this episode is excluded, the heart rate during dysfunction is 80 ± 14 beats/min. All but two episodes of left ventricular dysfunction occurred at rest while patients were sitting, with at least one episode clearly related to emotional stress. Two episodes were related to standing up and walking a short distance. In 16 of the 19 episodes of left ventricular dysfunction, left ventricular end-diastolic volume was within the variability of the measurement (±5%). The end-diastolic volume decreased by 5% to 10% in three episodes: this occurred in two patients while walking and in one patient during supraventricular tachycardia. In all episodes, the decrease in left ventricular ejection fraction was accompa-

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Table 2. Increases in Left Ventricular Ejection Fraction >0.10 With Ventricular Function Monitoring During Routine Activity in 23 Patients

	Transient Left Ventricular Dysfunction	
	Present (n = 12)	Absent (n = 21)
No.	9	14
No. of episodes/patient	3.1 ± 2.2	3.5 ± 2.4
Duration/episode (min)	5.7 ± 4.1	7.1 ± 4.3
Δ LVEF	0.13 ± 0.04	0.12 ± 0.03
Δ HR (beats/min)	14 ± 11	10 ± 10

HR = heart rate; Δ = change in; other abbreviations and definitions as in Table 1.

nied by an increase in end-systolic volume (mean 11 ± 8%, $p < 0.001$).

Increase in left ventricular function during monitoring (Table 2). During routine activity, 23 patients demonstrated a total of 77 episodes of a transient increase in ejection fraction ≥0.10. In normal subjects, this increase in ejection fraction lasting >1 min represented a major augmentation in left ventricular ejection fraction not observed with minimal activity. These episodes were usually associated with activity and an in increase in heart rate (12 ± 10 beats/min).

Submaximal bicycle exercise (Tables 3 and 4). Thirty-two of the 33 patients performed submaximal bicycle exercise testing; one patient could not participate because of previous knee surgery. The hemodynamic responses during submaximal supine bicycle exercise are listed in Table 3, and are compared with the ejection fraction responses during monitoring with routine activity in Table 4. In contrast to the data obtained with routine activity, only 2 of 32 patients demonstrated a decrease in ejection fraction during bicycle exercise ($p < 0.01$). Of the 12 patients with transient left ventricular dysfunction during routine activity, none demonstrated a decrease in ejection fraction ≥0.05 with bicycle exercise, 1 had an increase in ejection fraction ≥0.05, 10 had no change in ejection fraction (within ±0.04) and 1 was unable to exercise. Of the 21 patients without transient decreases in ejection fraction during routine activity, 2 had a decrease in ejection fraction, 12 showed no change and 7 had an increase in ejection fraction with bicycle exercise. Only two patients developed new or more severe regional wall motion abnormalities with exercise; one of these patients demonstrated left ventricular dysfunction during routine activity.

Table 3. Hemodynamic Response During Submaximal Supine Bicycle Exercise Testing

	Transient Left Ventricular Dysfunction	
	Present (n = 12)	Absent (n = 21)
Rest LVEF	0.52 ± 0.12	0.51 ± 0.13
Peak exercise LVEF	0.53 ± 0.14	0.54 ± 0.15
Rest HR (beats/min)	73 ± 12	68 ± 10
Peak exercise HR (beats/min)	111 ± 24	111 ± 18
Rest BP (beats/min)	138/84	119/72*
Peak exercise BP	176/86	168/85
Exercise time (min)	5.3 ± 2.8	6.1 ± 2.0
Peak exercise work load (kp-m)	400 ± 209	438 ± 136
ECG ST segment depression	4	2
No exercise	1	0

*$p < 0.05$. ECG = electrocardiographic; other abbreviations and definitions as in Tables 1 and 2.

Table 4. Exercise Ejection Fraction and Results of Thallium-201 Stress Scintigraphy in Patients Undergoing Monitoring During Routine Activity

	Transient Left Ventricular Dysfunction	
	Present (n = 12)	Absent (n = 21)
Exercise radionuclide angiocardiography		
↑ in LVEF	1	7
Flat LVEF	10	12
↓ in LVEF	0	2
No exercise	1	0
Thallium-201		
Ischemia	2	8
No ischemia	7	9
No exercise	3	4

Flat, ↑ and ↓ = no significant change, increase and decrease, respectively, from baseline to peak exercise; Thallium-201 = submaximal exercise thallium-201 stress scintigraphy; other abbreviations and definitions as in Table 1.

Thallium-201 treadmill exercise. Thallium-201 scintigraphy was performed on 26 of the 33 patients. Ten patients demonstrated a reversible defect indicating myocardial ischemia and 16 patients demonstrated no ischemia by thallium-201 imaging (fixed defect or no defect). No patient demonstrated increased thallium-201 lung uptake by visual analysis.

Follow-up and clinical course (Tables 5 and 6). Patients have been followed up for 21 ± 3.4 months (range 14 to 26). Eleven patients experienced a cardiac event; in seven the event occurred within 6 weeks. Four patients had a myocardial infarction (Q wave in two and non-Q wave in two); five patients developed unstable angina requiring treatment with either urgent coronary angioplasty or surgical revascularization. Two patients were hospitalized with unstable angina, but did not have anatomy suitable for coronary angioplasty; one of these patients died suddenly with documented myocardial infarction and ventricular fibrillation 4 weeks thereafter. There were no noncardiac deaths in the study patients. With the exception of rest blood pressure, there was no

Table 5. Clinical Characteristics and Exercise Variables for Patients With and Without Clinical Events at Follow-Up Study

	No Clinical Event (n = 22)	Clinical Event (n = 11)
Clinical variables		
Age (yr)	54 ± 12	59 ± 8
Peak CK (IU/liter)	1,639 ± 1,937	1,134 ± 573
PTCA	10	4
Previous MI	5	2
Anterior MI	10	5
Inferior MI	12	6
History of HTN	7	7
History of angina	7	2
Smoker at presentation	18	5
CHF at presentation	2	3
Exercise variables		
Rest LVEF	0.51 ± 0.13	0.52 ± 0.13
Peak exercise LVEF	0.55 ± 0.16	0.52 ± 0.11
Rest HR (beats/min)	71 ± 11	68 ± 10
Peak exercise HR (beats/min)	112 ± 18	108 ± 25
Rest BP (mm Hg)	122/73	134/82*
Peak exercise BP (mm Hg)	171/85	170/86
Exercise time (min)	6.2 ± 1.9	5.2 ± 3.0
ST segment depression	4	2
LVEF decrease ≥0.05	2	0

*$p < 0.05$. CHF = congestive heart failure; CK = creatine kinase; HTN = hypertension; PTCA = coronary angioplasty; other abbreviations as in Tables 1 and 2.

difference in clinical and exercise variables for the patients with and without a cardiac event.

Of the 11 patients with a cardiac event, 8 had an abnormal left ventricular ejection fraction response with monitoring during routine activity. Thus, although 8 of the 12 patients with an abnormal left ventricular ejection fraction response during routine activity had an event during follow-up, only 3 of 21 patients with no decrease in ejection fraction during routine activity had a subsequent cardiac event ($p < 0.01$).

There was no difference in the exercise response during bicycle exercise in patients with and without a cardiac event. Neither the two patients with a decrease in ejection fraction during bicycle exercise nor the two patients with new or more severe regional wall motion abnormalities at peak exercise had a cardiac event. One of 10 patients demonstrating a reversible defect on thallium-201 imaging had a subsequent cardiac event, and 8 of 16 patients with either a fixed defect or no defect had a subsequent cardiac event (p = NS). Two of the seven patients not performing thallium-201 treadmill exercise experienced a cardiac event. The clinical characteristics and exercise variables for the patients with and without a cardiac event are shown in Table 5.

Table 6. Relation of Ventricular Function Monitoring During Routine Activity, Bicycle Exercise and Thallium-201 Scintigraphy to Clinical Events at Follow-Up Study

	Cardiac Event (n = 11)	No Cardiac Event (n = 22)
VEST		
Abnormal	8	4
Normal	3	18*
Exercise radionuclide angiocardiography		
↓ in LVEF	0	2
Flat LVEF	10	12
↑ in LVEF	0	8
No exercise	1	0
Thallium-201		
Ischemia	1	9
No ischemia	8	8
No exercise	2	5

*$p < 0.01$. VEST = ventricular function monitoring during routine activity; other abbreviations and definitions as in Tables 1 and 4.

Discussion

This study demonstrates that transient episodes of silent left ventricular dysfunction can be detected during routine predischarge hospital activity in patients treated with thrombolytic therapy for acute myocardial infarction. We hypothesize that these episodes of left ventricular dysfunction reflect silent myocardial ischemia. Neither submaximal bicycle exercise radionuclide angiocardiography nor exercise thallium-201 scintigraphy predicted clinical outcome or ventricular function response during normal activity. Most episodes of ventricular dysfunction occurred at rest or with minimal increases in heart rate and blood pressure, and most patients did not demonstrate an ischemic response during exercise testing. However, only a small number of patients were studied. Before these data are applied to a larger group, a greater number of patients must be studied, allowing analysis of potential variables such as medications including beta-blockers, coronary angioplasty and other modes of treatment.

Absence of electrocardiographic changes. The normal left ventricular response to various physiologic circumstances has been documented with this technique (13). A good correlation has been described (14,15) between VEST and gamma camera measurements at rest and during exercise. Changes in ejection fraction recorded by the VEST during exercise are very reproducible at repeat testing in the same individuals (Bairey, personal communication). Tamaki et al. (14) reported 36 episodes of left ventricular dysfunction in 16 of 39 ambulatory patients with stable coronary artery disease during an average of 2.6 ± 1.3 h of monitoring. Seventeen (47%) of these episodes in 11 patients occurred without symptoms or ECG changes. Breisblatt et al. (16) noted 56

abnormal events in 23 patients with recent myocardial infarction who did not undergo thrombolytic therapy. Left ventricular dysfunction occurred during routine activity, exercise and mental stress, and 75% of these episodes also were both clinically and electrocardiographically silent.

In our study, a decrease in ejection fraction during routine activity was a relatively common event. Most of these episodes were silent; only one patient had ECG changes and chest pain during monitoring. This finding may in part be related to the relatively small number of patients studied and the relatively brief monitoring period, but is consistent with the studies cited (14,16). In addition, Rozanski et al. (30) reported ischemic ECG changes in only 23% and chest pain in 17% of patients developing regional wall motion abnormalities during mental stress (30). These and our results are consistent with prior studies (7–11,31–33) demonstrating that exercise radionuclide imaging data may be more sensitive markers of myocardial ischemia than either exercise-induced chest pain or ST segment changes. However, it should be noted that 24 h Holter monitoring for ST segment changes was not routinely performed in our study.

Potential mechanisms. The mechanism underlying a decrease in ejection fraction during normal activity does not appear to be related to an increased myocardial oxygen requirement. Most episodes occurred at rest, with no significant change in heart rate. Furthermore, patients demonstrating left ventricular dysfunction during routine events were capable of increasing ejection fraction at other times when heart rate increased, reflecting greater demand. These data are similar to those from other ambulatory ECG studies (27–29) in which silent ischemia was frequently not accompanied by increases in heart rate. Significant changes in both left ventricular ejection fraction and regional wall motion have been shown to occur during mental stress in normal subjects and patients with coronary artery disease (34,28). In our laboratory, normal volunteers undergoing Stroop color word mental stress had a 0.13 increase in ejection fraction measured with the nuclear probe, with an associated increase in heart rate of 26 beats/min (34). These data indicate that ejection fraction may increase significantly out of proportion to an increase in heart rate during mental stress and low level exercise. Thus, it appears that a decrease in coronary supply can be assumed in these patients, causing transient silent myocardial ischemia. This could be caused by transient increased vasoreactivity, platelet aggregation or occlusive thrombus formation alone or in combination. Some changes in left ventricular ejection fraction in our study may have been caused by unrecognized mental stress, a phenomenon more likely to occur during routine activity than with exercise. It is also possible that these episodes may be related to less well defined biochemical or mechanical processes occurring after thrombolytic therapy or in reperfused myocardium. Ambulatory blood pressure measurements were not obtained while the patients were wearing the VEST; thus, changes in ejection fraction occurring as a result of changes in afterload cannot be excluded as a mechanism for left ventricular dysfunction. Because monitoring was started at the same time for all patients, the influence of circadian rhythm was not a variable (35,36). Transient left ventricular dysfunction occurred as frequently in patients with as without recent coronary angioplasty.

Practical aspects and clinical implications. The practical limitations to this technique do not relate to the weight of the detector or the electronic ware. Patients who did not tolerate the VEST for the full study stated that the garment was too constricting and uncomfortable. Positioning the VEST detector at present requires the use of an imaging gamma camera. Ejection fraction should be obtained with a gamma camera so that a background factor can be determined for calculation of VEST ejection fraction.

Our data extend observations on silent ischemia to include patients treated with thrombolytic therapy for acute infarction. Patients with episodes of apparent silent left ventricular dysfunction had a poorer clinical outcome. In this study, ventricular function monitoring during routine hospital activity provided prognostic information not available from either exercise radionuclide angiocardiography or thallium-201 scintigraphy. The exercise left ventricular performance results were somewhat surprising, particularly in view of the ambulatory monitoring results. This may in part be related to the concomitant use of beta-blockers or other medication. However, our exercise results are consistent with the more generalized data from the TIMI II trial (37). Although additional larger-scale studies are necessary, the identification of silent left ventricular dysfunction during routine predischarge ambulatory activity may be a valuable method of assessing silent ischemia in this patient group. This new technique may be useful for risk stratification in patients after thrombolytic therapy and possibly other groups of patients with coronary artery disease.

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